AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1(Original). A method for generating a non-human mammalian model of an autoimmune disorder, said method comprising the steps of:

(a) producing intermated progeny of a first and a second transgenic non-human mammal of the same species, wherein said first mammal expresses a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) and said second mammal expresses a selected peptide that binds to said TCR, which selected peptide is selectively expressed by MHC class II positive antigen presenting cells (APC) of said second mammal; and

(b) selecting from said progeny those mammals that co-express said TCR and said selected peptide,

wherein said selected progeny develop an autoimmune disorder.

2(Original). The method according to claim 1, wherein said model is a high penetrance model of said disorder and wherein said selected peptide is a naturally-occurring, recombinant or synthetic MHC class II-restricted T cell determinant that specifically binds with high affinity to said TCR.

3(Original). The method according to claim 2, wherein at least 50% of said progeny before selection develop said autoimmune disorder.

4(Original). The method according to claim 2, wherein said TCR is the TS1 TCR and said determinant is A/PR/8 hemagglutinin (HA) peptide S1.

5(Original). The method according to claim 4, wherein said first mammal is a transgenic mouse that expresses MHC class II-restricted TCR with high affinity for an A/PR/8 hemagglutinin (HA) peptide S1 and said second mammal is a transgenic mouse that expresses DNA encoding the influenza A/PR/8 HA peptide S1 operably linked to a functional fragment of the MHC class II I-Eα promoter.

6(Original). The method according to claim 1, wherein said model is a low penetrance model of said disorder and wherein said selected peptide is a naturally-occurring, recombinant or synthetic protein or peptide fragment that binds with low affinity to said TCR.

7(Canceled).

8(Original). The method according to claim 6, wherein said TCR is the TS1(SW) TCR and said peptide is A/PR/8 hemagglutinin (HA) peptide S1.

9(Original). The method according to claim 8, wherein said first mammal is a transgenic mouse that expresses a MHC class II-restricted TCR with high affinity for an synthetic mutant S1 analog of A/PR/8 HA, but with low affinity for the native A/PR/8 HA S1 peptide; and wherein said second mammal is a transgenic mouse that expresses DNA encoding the native influenza A/PR/8 HA S1 peptide operably linked to a functional fragment of the MHC class II I-Eα promoter.

10(Original). The method according to claim 9, wherein said mutant analog is an HA peptide SEQ ID NO: 2 differing by two amino acids from said A/PR/8 HA S1 peptide SEQ ID NO: 1.

11(Original). The method according to claim 1, wherein in said second mammal a first nucleic acid sequence encoding said selected peptide is operably linked to a second

nucleic acid sequence that directs expression of said first nucleic acid sequence selectively to MHC class II positive cells.

12(Currently Amended). The method according to claim 11, wherein said second nucleic acid sequence encodes the MHC class II I ~~E~~ E-α gene promoter, non-MHC class II sequences involved in expression of the invariant chain, non-MHC class II H2-M promoter, the Dec205 promoter and the Cd11c promoter.

13(Canceled).

14(Original). The method according to claim 1, wherein said autoimmune disorder is inflammatory arthritis.

15(Original). The method according to claim 14, wherein said disorder is characterized by inflamed joints with bone resorption, mononuclear cell infiltrates and pannus formation.

16(Canceled).

17(Original). A non-human mammalian model of an autoimmune disorder, produced by the method of claim 1.

18-19(Canceled).

20(Original). A transgenic non-human mammal that expresses a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) and expresses a selected peptide that binds to said TCR, which selected peptide is selectively expressed by MHC class II positive antigen presenting cells (APC), wherein said mammal develops the phenotypic symptoms of an autoimmune disorder.

21-25(Canceled).

26(Original). A recombinant mammalian cell containing at least one transgene comprising a first nucleic acid sequence that encodes a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) operably linked to regulatory sequences directing its expression; and a second nucleic acid sequence that encodes a selected peptide that binds to said TCR, operably linked to a sequence that directs expression of said selected peptide selectively to MHC class II positive antigen presenting cells (APC).

27-28(Canceled).

29(Original). A method for producing a transgenic non-human mammalian model of an autoimmune disorder, said method comprising introducing at least one transgene comprising a first nucleic acid sequence that encodes a major histocompatibility (MHC) class II-restricted T cell receptor (TCR) operably linked to regulatory sequences directing its expression; and a second nucleic acid sequence that encodes a selected peptide that binds to said TCR, operably linked to a sequence that directs expression of said selected peptide selectively to MHC class II positive antigen presenting cells (APC) into a fertilized egg, wherein said egg is transplanted into a pseudopregnant mammal and developed to term, and wherein said at least one transgenic offspring contains said transgene and is bred to form a transgenic mammal having said autoimmune disorder.

30-32(Canceled).

33(Original). A cell culture comprising cells derived from tissues of a transgenic non-human mammal of ~~any of claims~~ claim 20 ~~to 25~~.

34(Original). A method of screening a compound for the ability to effect symptoms of an autoimmune disorder, comprising the steps of:

(a) administering a test compound to a mammalian model of autoimmune disorder selected from the mammal of claim 20 ~~any of claims 17 to 25~~; and

(b) comparing the severity of said symptom in the mammalian model (a) to a control mammal to which said test compound was administered.

35(Canceled).

36(Original). A method of identifying a gene product responsible for the development of autoimmune disorders comprising the steps of:

identifying expression levels of a gene product of a mammalian model of autoimmune disorder selected from the mammal of claim 20 ~~any of claims 17 to 25~~;

comparing expression of said gene product with the expression of the same or analogous gene product in a control mammal; and

determining a difference in the expression of said gene product, wherein the absence, upregulation or downregulation of said gene product between said model and said control.

37-38(Canceled).

39(Currently Amended). A method for identifying a biochemical marker of an autoimmune disorder comprising:

comparing the T cells or MHC class II positive APC of a mammalian model of claim 20 with a high genotypic penetrance of said disorder with the T cell of ~~a~~ said mammalian model with a low genotypic penetrance of said disorder; and

identifying a biochemical marker present on T cells or MHC class II positive APC of one model that is not present the T cells or MHC class II positive APC of the other model;

wherein the presence of said marker on said high penetrance model and absent on said low penetrance model or the absence of said marker on said high penetrance model and its presence on said low penetrance model is an indicator of a high likelihood of the development of said autoimmune disorder.

40-45(Canceled).